

NORBERT KOTHE ET AL.
USSN 10/030,801
Reply to Office Action dated March 29, 2004
Amendment of September 29, 2004

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for fractionating plasma or serum, wherein said method comprising subjecting a starting solution, containing plasma or serum, ~~is subjected to a~~ fractionation by hydrophobic interaction chromatography without rivanol precipitation, wherein during said hydrophobic interaction chromatography and, by using a stepwise salt gradient, is employed to obtain (at least) one immunoglobulin-containing fraction and one albumin-containing fraction ~~are obtained~~.
2. (Currently Amended) The method of claim 1, wherein the starting solution contains a plasma or serum of human ~~or animal origin is used as starting material~~.
3. (Previously Presented) The method of claim 1, wherein an ammonium sulfate gradient is used for the chromatography.
4. (Currently Amended) The method of claim 3, wherein the chromatography comprises a first fractionation step ~~commences~~ at a high concentration of ammonium sulfate,

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~~which is lowered in the next step of the~~ and a second fractionation step at a lower
concentration of ammonium sulfate.

5. (Currently Amended) The method of claim 34, wherein the high concentration of ammonium sulfate is between 0.6 and not more than 1.4 moles/L and the ~~low ammonium~~ lower concentration is between 0 and 0.4 moles/L.

6. (Currently Amended) The method of claim 34, wherein the high concentration of ammonium sulfate ~~buffer~~ is 0.7 to 1 moles/L, ~~which is lowered to~~ and the lower concentration
is between 0 to 0.3 moles/L.

7. (Currently Amended) The method of claim 1, wherein the starting solution and the chromatography solid phase are adjusted to ~~the a~~ desired high salt gradient concentration at the start of the fractionation.

8. (Currently Amended) The method of claim 1, wherein the starting solution
contains plasma, from which the clotting factors of the PPSB complex ~~were~~ have been removed
~~by a known procedure, is used as starting material.~~

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9. (Currently Amended) The method of claim 1, wherein the starting solution contains plasma or serum from which clotting factor VIII is has been removed from the starting material by a known procedure, and this starting material is used for the preparative fractionation.

10. (Currently Amended) The method of claim 2, wherein the starting solution contains polyvalent human plasma is used as a starting material.

11. (Currently Amended) The method of claim 2, wherein the starting solution contains selected human plasma, selected with respect to viral, bacterial or antibodies, directed against cellular antigens, is used as starting material.

12. (Currently Amended) The method of claim 1, wherein, after the obtaining a first fraction, two further fractions are obtained by means of step gradients.

13. (Previously Presented) The method of claim 12, wherein, after the first fraction, the fractionation commences with an ammonium sulfate buffer having a concentration of 0.4 to 0.1 moles/L, which is then lowered to less than 0.1 to 0 moles/L.

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14. (Currently Amended) The method of claim 1, wherein phenyl-substituted or alkyl-substituted phases, based on copolymers of glycidyl methacrylate and ethylene glycol dimethacrylate, copolymers of polystyrene or divinylbenzene or silica, coated with dextran or polymers, are used as hydrophobic interaction solid phase.

15. (Currently Amended) The method of claim 14, wherein copolymers of glycidyl methacrylate and ethylene glycol dimethacrylate are used as hydrophobic interaction solid phase.

16. (Currently Amended) The method of claim 14, wherein the fractionation employs a high concentration of ammonium sulfate buffer is of 0.8 to 1.0 moles/L and the a lowered concentration of ammonium sulfate is of 0.3 to 0 moles/L.

17. (Currently Amended) The method of claim 16, wherein the a first fraction is obtained at an ammonium sulfate concentration of 0.9 moles/L and, after that, a step gradient is employed, the ammonium sulfate concentration initially being 0.3 moles/L and then lowered to 0 moles/L.

18. (Currently Amended) The method of claim 1, wherein the a first fraction obtained is worked up ~~in a known manner~~ and therapeutically usable antithrombin III, transferrin and/or albumin are obtained.

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19. (Currently Amended) The method of claim 18, wherein the first fraction obtained is worked up by affinity chromatography followed by anion exchange chromatography and virus inactivation as well as ~~the usual~~ filtering, concentrating and sterilizing steps.

20. (Currently Amended) The method of claim 1, wherein the a second fraction obtained is worked up ~~in a known manner~~ and therapeutically usable immunoglobulin, especially IgG, is obtained.

21. (Currently Amended) The method of claim 20, wherein the second fraction obtained is worked up by anion exchanger chromatography, virus inactivation, octanoic acid treatment, as well as cation exchanger chromatography and ~~the usual~~ filtering, sterilizing and concentrating steps into a compatible immunoglobulin G preparation.

22. (Canceled)

23. (Currently Amended) The method of claim ~~22~~29, wherein, after the first fraction is eluted, the chromatographic column is treated with a step gradient and a second and third fraction are obtained ~~in this manner~~.

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24. (Currently Amended) The method of claim ~~2229~~, wherein, after each recycling cycle, the interaction chromatography solid phase is treated with sodium hydroxide solution ~~from a reservoir 3~~.

25. (Currently Amended) The method of claim ~~2229~~, wherein the first fraction obtained is worked up ~~in a known manner~~ and therapeutically usable antithrombin III, transferrin and/or albumin are obtained.

26. (Currently Amended) The method of claim ~~2229~~, wherein the second fraction obtained is worked up ~~in a known manner~~ and therapeutically usable immunoglobulin, ~~especially~~ IgG, is obtained.

27. (Canceled)

28. (New) The method of claim 20, wherein the therapeutically usable immunoglobulin is IgG.

29. (New) A recycling method for fractionating plasma or serum, said method comprising the following steps:

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- a) subjecting a starting solution, containing plasma or serum, to a fractionation by hydrophobic interaction chromatography in a chromatographic column without rivanol precipitation to obtain a first fraction comprising albumin and a second fraction comprising immunoglobulin, said first fraction also containing a permeate comprising ammonium sulfate;
- b) separating the permeate from the first fraction; and
- c) recycling the permeate to a subsequent step a).

30. (New) The method of claim 26, wherein the therapeutically usable immunoglobulin is IgG.

31. (New) A therapeutic method comprising the following steps:

- a) carrying out the method of claim 1 to obtain a therapeutically usable immunoglobulin preparation, an antithrombin III preparation, an albumin preparation or a transferrin preparation; and

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- b) administering a therapeutically effective amount of at least one of said preparations to a patient in need thereof.

32. (New) A therapeutic method comprising the following steps:

- a) carrying out the method of claim 29 to obtain a therapeutically usable immunoglobulin preparation, an antithrombin III preparation, an albumin preparation or a transferrin preparation; and
- b) administering a therapeutically effective amount of at least one of said preparations to a patient in need thereof.